REMARKS

Overview

Claims 1-8, 10-16, 19-27 and 29-32 are pending in this application. Claims 9, 17, 18, and

28 have been cancelled. Claims 1, 2, 3, 15, 16, 19, 20, 21, 22, and 23 have been amended.

Claims 30-32 are new. The present response is an earnest effort to place all claims in proper

form for immediate allowance. Reconsideration and passage to issuance is therefore respectfully

requested.

Issues Regarding Elections/Restrictions

Claims 9 and 17-18 had previously been withdrawn from consideration. This amendment

cancels claims 9 and 17-18.

Issues Under 35 U.S.C. § 102

Claims 1, 3-5, 19-20, 22-23, and 25-27 have been rejected under 35 U.S.C. § 102(a) as

being anticipated by Edwards et al. (BMC Bioinformatics (2000) vol. 1:1, pages 1-10).

Claim 1 has been amended to specifically refer to the "logic constraints" previously

presented in claim 2. As the Examiner has already recognized, Edwards does not disclose the

"logic constraints" of the claimed invention, this rejection to claim 1 must be withdrawn. As

claims 3-5 depend from claim 1, these rejections must also be withdrawn.

Similarly, claim 19 has been amended to specifically refer to "logic constraints". As

Edwards does not disclose this limitation, this rejection to claim 19 must also be withdrawn. As

claims 20 and 22 depend from claim 19, these rejections must also be withdrawn.

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Claim 23 has been amended to incorporate the limitations of now cancelled claim 28. The Examiner previously indicated that claim 28 contains allowable subject matter. Therefore, the Examiner should now find claim 23 allowable. As claims 25-27 depend from claim 23, the Examiner should also find these claims allowable.

Issues Under 35 U.S.C. § 103

The Examiner has rejected claims 2, 6-8, 10-16, 21 and 24 under 35 U.S.C. § 103(a) as being unpatentable over Edwards et al. as applied to claims 1, 3-5, 19-20, 22-23, and 25-27 above, and further in view of Schilling et al (PNAS (4/1998) vol. 95, pp. 4193-4198). The combination of Schilling and Edwards is deficient and therefore these rejections are respectfully traversed.

To assist in the Examiner's understanding of the claimed invention and the patentable differences between what is claimed and the prior art references relied upon by the Examiner, the Declaration of Dr. Christophe Schilling, Ph.D. is provided. It is of particular note that Christophe Schilling is the same Christophe Schilling who authored the Schilling reference relied upon by the Examiner and that he interprets the Schilling reference differently than the Examiner. Thus, it is hoped that the Examiner will find the Declaration particularly helpful and persuasive.

In particular, the methodologies described in Edwards and Schilling, alone or in combination, are significantly and fundamentally different from that which is claimed in the present application.

Fundamentally, the claimed invention approaches flux balance analysis in a different way. Prior art references such as Schilling use stoichiometric mass balances of the metabolic network

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and cellular composition information to identify boundaries for the flux distribution available to the cell. Schilling further describes how the mass balance constraints that govern a biochemical reaction network allow for the translation of the functional definition of biochemical pathways to a linear algebra problem. This is a fundamentally different approach then the use of logic constraints as claimed. The use of logic constraints allow, for example, one to ensure that when in response to environmental changes, the metabolic network shifts from one steady-state to another, up or down changes in metabolite concentration are consistent with up or down changes in reaction fluxes.

It is further observed that the Examiner appears to equate linear programming with mixed-integer linear programming. Although there is similarity in the names of these types of mathematical approaches, the approaches as used in the context of the present invention are significantly different resulting in a different model, different results, and different advantages. In particular, a linear programming approach deals with continuous variables and although may be useful in determining bounds of a particular reaction, is not useful in providing an overall flux balance analysis model. In contrast, the mixed-integer linear programming approach allows some variables to be discrete values and allows one to consider hundreds of different reactions at the same time and explore numerous scenarios based on various on/off decisions (i.e., whether a reaction is on or is not on). Thus, although there is a similarity of language, the use of linear programming in Schilling and Edwards is significantly and fundamentally different from what is claimed. Therefore, as stated by Dr. Schilling, one skilled in the art would not have considered the claimed invention to be obvious with respect to the combination of Schilling and Edwards. Therefore, for all these reasons and as articulated in the Declaration of Dr. Schilling, these rejections to claims 6-8, 10-16, 21 and 24 should also be withdrawn.
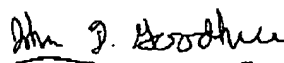
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New Claims

Claims 30-32 are new and do not introduce new matter. It is observed that claim 30 is similar to claims 6 and 14. Similarly, claims 31 and 32 are similar to claims 15-16.

Conclusion

Applicant is a small entity; therefore, please charge Deposit Account 26-0084 the amount of $395.00 to cover the costs associated with the filing of this RCE. This is also a request to extend the period for filing a response in the above-identified application for one month from March 16, 2005 to April 16, 2005. Therefore, please charge Deposit Account number 26-0084 in the amount of $60.00 to cover the cost of the one month extension. Any deficiency or overpayment should be charged or credited to Deposit Account 26-0084. No other fees or extensions of time are believed to be due in connection with this amendment; however, consider this a request for any extension inadvertently omitted, and charge any additional fees to Deposit Account No. 26-0084.

Respectfully submitted,

JOHN D. GOODHUE, Reg. No. 47,603
McKEE, VOORHEES & SEASE, P.L.C.
801 Grand Avenue, Suite 3200
Des Moines, Iowa   50309-2721
Phone No: (515) 288-3667
Fax No: (515) 288-1338
CUSTOMER NO: 27407
Attorneys of Record

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Enclosure: Declaration

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